Applicants acknowledge with appreciation the withdrawal of the rejection of claims 15-17 under 35 U.S.C. § 112, first paragraph; the withdrawal of the rejection of claims 1, 2, 5-7, 9-12, and 15-17 under 35 U.S.C. § 112, second paragraph; the withdrawal of the rejection of claims 1, 2, 5-7, and 9-12 under 35 U.S.C. § 102(a)/103 over Arya *et al.*; the withdrawal of the rejection of claims 1, 2, 5-7, and 9-12 under 35 U.S.C. § 102(e)/103 over Levy; and the withdrawal of the rejection of claims 15-17 under 35 U.S.C. § 102(b) over Wain-Hobson *et al.*

The specification is objected to and claims 23-31 are rejected under 35 U.S.C. § 112, first paragraph, as the disclosure is allegedly not commensurate with the scope of the claims. Applicants respectfully traverse the rejection.

It is alleged that the specification does not provide guidance as to the nucleotide sequence encompassed by the claimed invention. The Examiner states that one having skill in the art identifying HIV molecular clones from a different source would not know if he were in possession of the claimed invention. In support of the enablement rejection, the Examiner asserted that the Lentiviridae display considerable genomic heterogeneity and that HIV-1 exists as a quasispecies, or subpopulation of genetic variants. (Office Action at 3; *citing* Holland *et al.*, Curr. Topics Micro. Immunol. 176:1-120 (1992); Goodenow *et al.*, J. Acquir. Immune Defic. Syndr. 2:344-352 (1989).) Therefore, the Examiner alleges that "any particular restriction fragment will contain a unique nucleotide sequence depending upon the source of the clone." (Office Action at 4.)

However, enablement is to be determined as of the filing date. In re Koller, 204 U.S.P.Q. 702, 706 (C.C.P.A. 1980); In re Hogan, 194 U.S.P.Q. 527, 537 (C.C.P.A. 1977). Indeed, later

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discovery of unknown variations does not render the original claims non-enabled. Hogan, 194 U.S.P.Q. at 537. Otherwise, "the opportunity for obtaining a basic patent upon early disclosure of a pioneer invention would be abolished." Hogan, 194 U.S.P.Q. at 537.

This application is a continuation of S.N. 08/384,248, filed February 6, 1995, which is a continuation of S.N. 08/052,727, filed April 27, 1993, which is a continuation of S.N. 07/499,210, filed March 19, 1990, which is a continuation of S.N. 06/771,230, filed August 30, 1985, which is a continuation-in-part application of S.N. 06/706,562, filed February 28, 1985, which is a continuation-in-part application of S.N. 06/558,109, filed December 5, 1983. In addition, Applicants claim the benefit of the foreign priority document, GB 84 23659, filed September 19, 1984, which was presented to the Examiner in the Response and Amendment of March 28, 1996. Holland *et al.* and Goodenow *et al.* were published in 1992 and 1989, respectively, long after even the last parent CIP of this case was filed. Thus, as in Hogan, Applicants' original claim covered all known variations of the pioneering claimed subject matter. These variations were enabled by the specification as of the filing date. Other variations of the HIV-1 isolates were discovered after Applicants' invention. Therefore, the Examiner cannot reject the claims under 35 U.S.C. § 112, first paragraph, as allegedly being too broad, since Holland *et al.* and Goodenow *et al.* were not applicable as of the time of filing of even the last parent CIP of this case.

Furthermore, the use of standard experimental models has often been recognized as supporting broader claims for purposes of 35 U.S.C. § 112, first paragraph. See, e.g., In re

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Jolles, 206 U.S.P.Q. 885, 890-91 (C.C.P.A. 1980); In re Hartop, 135 U.S.P.Q. 419, 425-26 (C.C.P.A. 1962). The specification utilizes LAV, a standard experimental strain and model for HIV-1 isolates at the time the claimed invention was made. As in the case of standard experimental models, at the time of this application, one skilled in the art would have expected the results obtained from LAV to be generalizable across other HIV-1 strains.

Indeed, the specification supports this position, for example, at page 7, where Applicants teach using pLAV 13, a cDNA clone of LAV, in hybridization assays with LAV RNA from different sources. Therein Applicants teach that LAV RNA was detected using the pLAV 13 as a probe when contacted with LAV from different sources, such as normal T cells, B-cell LAV-producing lines, CEM cells, and LAV from the bone marrow culture from a hemophiliac with AIDS. Thus, it is apparent that at the time the claimed invention was made, the inventors believed that the claimed invention was useful for any HIV-1 isolates.

Moreover, Applicants submit that the Examiner confuses the issue of variability among HIV isolates. Lentiviruses are members of the family of the Retroviruses, which encompass the group of oncoviruses and spumaviruses. Lentiviruses include HIV-1, HIV-2, SIV, human spuma or foamy retrovirus, Rous Sarcoma virus, bovine leukemia virus, mouse mammary tumor virus, infectious anemia virus, hamster intracisternal A-type particle, feline immunodeficiency virus, and ovine maedi/visna virus, for example. (Vartanian and Wain-Hobson, AIDS in Africa, Raven Press, Ltd.: New York (1994)(Exhibit 1), pages 21-46.) Of course there exists "genomic heterogeneity" between lentiviruses in view of the different types of viruses included in this class

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as well as their infectivity in different host species. However, within the HIV family itself, only two types of HIV have been isolated thus far: HIV-1 and HIV-2. While philogenetic studies have permitted the discovery of variants of HIV-1 and HIV-2, these variants are nonetheless bound by their biological properties to the HIV-1 and HIV-2 families. Indeed, Vartanian and Wain-Hobson provide the biological overview of HIV-1 in the attached Exhibit 1. Thus, the "variability" among HIV viruses does not render an HIV-1 variant a non-member of the HIV-1 family.

However, in an effort to expedite prosecution, Applicants have amended the claims to delete "having the sequence" and recite that the DNA fragments "corresponds to the fragment." In view of the foregoing remarks and amendments, Applicants respectfully request that this rejection be withdrawn.

Claims 23-31 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter, which applicants regard as the invention.

The Examiner states that the recitation of "at approximately" precludes identification of the precise location of the restriction sites. Applicants respectfully traverse the rejection.

A term of degree must be analyzed based on whether the specification provides a standard for measuring that degree and, if not, whether one of ordinary skill in the art, in view of the prior art and the status of the art, would be reasonably apprised of the scope of the invention. M.P.E.P. 2173.05(b). Here, the specification teaches the approximate restriction sites of LAV for the various restriction enzymes at pages 4-5. As is apparent from the disclosure at page 4, there

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would be no mystery for determining whether or not a particular *Hin*dIII restriction site at approximately nucleotide 0, 520, 1100, 7850, and 9250 is within the scope of the claimed invention. In fact, even where restriction sites appear to be close for a particular enzyme, such as *Kpn*I at approximately nucleotides 3500 and 3900, the specification further addresses that the approximate sites were estimated within 200 base pairs. *See* specification, page 4, line 1. Accordingly, one having ordinary skill would be capable of determining the site to which the claimed invention relates. Thus, based upon the teachings in the specification and the skill in the art, one having ordinary skill in the art would be capable of assessing whether or not a particular site where DNA is cut by a particular restriction enzyme is or is not within the scope of the claimed invention.

In addition, the courts have held that relative terminology such as "approximately" and "about" are acceptable terminology in claims. For example, in Amgen, Inc. v. Chugai Pharmaceutical Co. Ltd., the Federal Circuit stated that "about" is acceptable terminology in appropriate situations. 18 U.S.P.Q.2d 1016, 1031 (Fed. Cir. 1991) *citing* W.L. Gore & Assocs., Inc. v. Garlock, Inc., 220 U.S.P.Q. 303, 316 (Fed. Cir. 1983). Therefore, in view of the foregoing, Applicants respectfully request withdrawal of the instant rejection.

Applicants submit that the foregoing remarks should overcome all outstanding rejections and place this application in condition for allowance. In the event that the Examiner disagrees, he is invited to call the undersigned to discuss the remaining issues.

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Applicants respectfully request that this Amendment under 37 C.F.R. § 1.116 be entered by the Examiner. Applicants submit that the proposed amendments do not raise new issues or necessitate the undertaking of any additional search of the art by the Examiner. Therefore, this Amendment should allow for immediate action by the Examiner.

Moreover, Applicants submit that the entry of the Amendment would place the application in better form for appeal, should the Examiner dispute the patentability of the pending claims.

If there are any other fees due in connection with the filing of this response, please charge the fees to our Deposit Account No. 06-0916. If a fee is required for an extension of time under 37 C.F.R. § 1.136 not accounted for above, such an extension is requested and the fee should also be charged to our Deposit Account.

Respectfully submitted,

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By: _____
Kenneth J. Meyers
Reg. No. 25,146

Dated: November 4, 1996

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